SEP - 7 2005

K 052098

1.4 510(k) Summary of Safety and Effectiveness

1. Sponsor

IsoTis OrthoBiologics, Inc.
2 Goodyear, Suite B
Irvine, CA 92618
U.S.A

Contact Person: Paul Doner
Telephone: 949 855-7168
Facsimile: 949 595-8711

Date Prepared: August 2, 2005

2. Device Name

Proprietary Name: Connexus, 0.5cc
Common/Usual Name: Bone Void Filler
Classification Name: Sec. 888.3045 Resorbable calcium salt bone void filler device.

3. Predicate Devices

Connexus (K050690, July 7, 2005)

4. Device Description

IsoTis OrthoBiologics is expanding the range of sizes previously cleared in 510(k) K050690 to include Connexus, 0.5cc. The intended use of this additional size does not change from that previously cleared.

Connexus is derived from selected donated human bone tissue that has been processed into particles. The bone particles are subsequently demineralized using a hydrochloric acid process. The demineralized bone matrix (DBM) is combined with an inert reverse phase carrier and formulated to a putty-like consistency.

The carrier is a solution of polyethylene oxide polypropylene oxide block copolymer dissolved in water exhibiting reverse phase characteristics (i.e., an increase in viscosity as temperature increases).

5. Intended Use

For orthopedic applications as filler for gaps or voids that are not intrinsic to the stability of the bony structure. Connexus is indicated to be packed gently into bony gaps in the skeletal system as a bone graft extender and as a bone void filler of the extremities and pelvis. These defects may be surgically created or the result of traumatic injury to the bone.

6. Technological Characteristics and Substantial Equivalence

Connexus and its predicate devices are similar in design, materials of construction and function. The proposed and predicate devices are osteoconductive and osteoinductive. The Connexus product and its predicate devices provide an interconnected, porous scaffold and an environment for new bone ingrowth and stimulate bone growth. The only differences between the proposed device and its predicates are the percentage of demineralized bone and the inert carriers used. Connexus is provided sterile and for single patient use. The donor bone in the Connexus product meets the requirements of the AATB. Product safety and effectiveness is adequately supported by the substantial

equivalence information, materials data, and test results provided in this Premarket Notification.

- Viral Inactivation Validation
  The methods for processing the DBM contained in Connexus were evaluated for their viral inactivation potential. A select panel of viruses representing various virus types, sizes, shapes, and genomes were evaluated. The viral inactivation testing demonstrated suitable viral inactivation potential of the processing methods for a wide range of potential human viruses.

- Osteoinductivity Potential
  The osteoinductive potential of the DBM used in Connexus is determined via an *in vitro* assay. The assay measures the alkaline phosphatase activity of myoblast cells. The level of alkaline phosphatese induction is compared to positive and negative DBM controls. Results from the assay were correlated with results from implantation of DBM into an athymic rat muscle pouch. Analysis of these results shows that the *in vitro* assay has been validated against the *in vivo* athymic rat model and predicts with at least 95% confidence the *in vivo* osteoinductivity of the test material. 67 out of 67 test lots that passed the *in vitro* assay passed the *in vivo* athymic rat assay via confirmation of intramuscular bone formation.

  Each lot of DBM incorporated in the Connexus is evaluated for osteoinductive potential using an *in vitro* assay. Testing each lot of DBM assures that only DBM with ostoeinductive potential is used in Connexus. Although DBM used in the final product has been shown to be osteoinductive using an *in vitro* assay, the combination of DBM and inert carrier has not been evaluated for osteoinductivity; therefore, it is unknown to what extent the formulation components may alter the osteoinductivity character of the DBM. Additionally, it is unknown how osteoinductivity of the DBM component, measured via the *in vitro* assay, will correlate with human clinical performance of Connexus.

  Product Performance Testing
  Performance of Connexus has been evaluated in rabbit and sheep models by radiographic and histological methods for the indications specified in the Premarket Notification.

  These data substantiate Connexus Putty safety and effectiveness for the indications presented in this Premarket Notification.

1.5 Performance Standards

No performance standards applicable to Connexus bone void filler material have been adopted under Section 514 of the Act. Connexus complies where appropriate with the applicable requirement of the following voluntary/consensus standards:

- ISO 10993-1: Biological Evaluation of Medical Devices Part-1: Evaluation and Testing
- 21 CFR 1270, Human Tissue Intended for Transplantation
- United States Pharmacopeia (USP) XXVI – The National Formulary (NF) Specifications XXI
- United States Pharmacopeia (USP) XXVII – The National Formulary (NF) Specifications XXII
- ISO 11137:1997; Sterilization of Health Care Products – Requirements for Validation and Routine Control – Radiation Sterilization
- ASTM 1980 – 02:1999 (current edition approved Jan. 2002); Standard Guide for Accelerated Aging of Sterile Medical Device Packages
- American Association Standards for Tissue Banking, (10th Edition – printing date: April 2002)

Additionally, IsoTis OrthoBiologics' Quality System complies with the FDA Quality System Requirements (21 CFR 820), ISO 13485 and its facility is American Association of Tissue Banks (AATB) accredited.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

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Mr. Paul Doner
Director of Regulatory Affairs and Quality Assurance
IsoTis OthoBiologics Inc.
2 Goodyear, Suite B
Irvine, California 92618

Re: K052098
Trade Name: Connexus™, 0.5cc
Regulation Number: 21 CFR 888.3045
Regulation Name: Resorbable calcium salt bone void filler device
Regulatory Class: II
Product Code: MQV
Dated: August 2, 2005
Received: August 11, 2005

Dear Mr. Doner:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

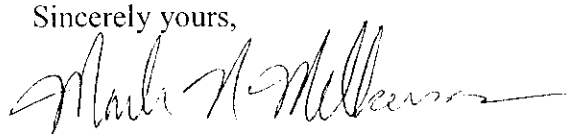
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-0120. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Mark Melkerson
Acting Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

1.3 Statement of Indications for Use

510(k) Number (if known):

Device Name: Connexus ™, 0.5cc

Indications for Use:

Connexus is an osteoinductive and osteoconductive bone filling material indicated:

For orthopedic applications as filler for gaps or voids that are not intrinsic to the stability of the bony structure. Connexus is indicated to be packed gently into bony gaps in the skeletal system as a bone graft extender and as bony void filler of the extremities and pelvis. These defects may be surgically created or from the result of traumatic injury to the bone.

Prescription Use __X____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (Part 21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NECESSARY)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of General, Restorative,
and Neurological Devices

510(k) Number K052098